

REMARKS

In response to the Office Action mailed August 14, 2003, Applicants submit the following Amendment and Response. Claims 275-281, 283-286, 291-308, and 315-326 have been amended. Claims 309-314 have been canceled. Claims 327-372, which roughly correspond to claims 275-326, have been newly added. Claims 275-308 and 315-372 remain pending. Support for these amendments can be found in the specification at, e.g., page 34, line 29 – page 36, line 19. Therefore, these amendments are made without the addition of new matter.

Specification

Several informalities in the disclosure were objected to by the examiner. Applicants have deleted the second comma on page 36, line 29 and page 37, line 1. Applicants have also amended the paragraphs beginning on page 15, line 5 and page 34, line 29 of the specification to define “CNA” as “cyclohexyl nucleic acids.” Therefore, applicants respectfully request withdrawal of these objections.

Information Disclosure Statement

As requested, copies of all but one of the non-U.S. Patent references have been provided. We will provide a copy of reference DN Miculka, C. et al., European BioPharmaceutical Review, 6/98, p. 52-57 as soon as possible. Applicants hereby request consideration of these references and the return of the initialed 1449s for these attached references. Applicants have also submitted herewith another Supplemental Information Disclosure Statement, which lists references cited in a

related International Search Report that were not included in previous Information Disclosure Statements.

35 U.S.C. § 112

Claims 275-326 were rejected as being allegedly indefinite under 35 U.S.C. § 112, second paragraph, for failing to particularly point out and distinctly claim the subject matter that applicants regard as the invention.

In particular, in claim 275, it is allegedly unclear whether the method steps modify a target nucleic acid as claimed. Applicants have amended claim 275 to delete “target nucleic acid.”

In addition, the terms “the nucleic acid” (line 2), “the action of the enzyme” (step a), “the mixture” (step b), line 1), and “the functioning” (step b), lines 1-2) allegedly lack antecedent basis. Applicants have amended claim 275 to provide correct antecedent basis for “a nucleic acid” in the first step. In addition, the terms “the action of the enzyme,” “the mixture,” and “the functioning” have been deleted.

Claim 293 was rejected as allegedly indefinite due to the phrase “contacting the conjugate with an RNAase H activity in the mixture.” Applicants have amended the claim to recite the step of “contacting the conjugate with a RNAase H enzyme.”

Claims 301-308 were rejected as allegedly indefinite due to the phrases “the point of activity” and “the point of conjugation.” These terms have been amended to “the modification” and “the attachment point.” Each of these terms has proper antecedent basis in independent claim 276 and the beginning of each dependent claim, respectively.

Claims 325 and 326 were rejected for containing certain trademark names for the dyes. The trademark names have been deleted and the chemical names have been added for some of the dyes.

Art Rejections

Claims 275-287, 289-290, 292, 297-314, 319-324, and 323-325 were rejected under 35 U.S.C. § 102(b), as being allegedly anticipated by Kool (USP 6,077,668). Claims 288 and 291 were rejected under 35 U.S.C. § 103(a), as being allegedly unpatentable over Kool in view of Zhang et al. (USP 5,876,924). Claim 293 was rejected under 35 U.S.C. § 103(a), as being allegedly unpatentable over Kool in view of Berninger et al. (USP 5,194,370). Claims 294-296 were rejected under 35 U.S.C. § 103(a), as being allegedly unpatentable over Kool in view of Nelson et al. (Methods in Enzymology, 1979, 68: 41-50). Claims 322 and 326 were rejected under 35 U.S.C. § 103(a), as being allegedly unpatentable over Kool in view of Mannigan et al. (USP 6,399,302).

Applicants respectfully assert that the prior art does not teach or suggest each and every limitation of the amended claims. In particular, Kool does not teach or suggest modifying “*a conjugate comprising a nucleic acid and a synthetic binding unit, wherein the synthetic binding unit is selected from the group consisting of pRNA, pDNA, and CNA.*” Although the examiner has cited Col. 13, line 57 – Col. 14, line 11 as describing pRNA, nowhere does Kool describe modifying a *conjugate*. In fact, in Col. 8, lines 61-65, Kool states that “[t]he circular oligonucleotide template ... used for DNA or RNA oligonucleotide synthesis is composed of a single nucleotide strand containing naturally occurring *or* modified nucleotides.” By use of the disjunction “or,” it is plain that Kool contemplated two alternative simple nucleotide strands, not conjugates containing both naturally occurring and modified nucleotides.

In addition, it would not be obvious from Kool to make or modify conjugates containing nucleic acids and pRNA, pDNA, and CNA because Kool describes a synthetic scheme that “is performed by combining a circular single-stranded oligonucleotide template with an effective polymerase and at least two types of nucleotide triphosphate, without the addition of auxiliary proteins, to yield an oligonucleotide multimer comprising multiple copies of a repeated oligonucleotide sequence.” (See Abstract) Kool therefore requires a polymerase to perform the techniques described in Kool. The synthetic binding units of the present invention “cannot be synthesized, amplified, modified, processed, ligated, fragmented or hydrolyzed by enzymes which are known from nucleic acid technology, such as polymerases, ligases, nucleases, restriction enzymes, etc.” (Specification, page 35, lines 26-29) Thus, because pRNA is not a substrate recognized by a polymerase enzyme, the conjugate suggested by the Examiner would not be amplified by the process described in Kool. Therefore, applicants respectfully request withdrawal of the rejections and reconsideration of the claims as amended.

Patent US 503
Attorney Docket: 612,406-014
(former L&L Ref: 264/217)

Applicants submit that the claims, as amended, are free of the cited art and are in position for allowance. Please charge Deposit Account No. **50-2862** for the 2-month extension fee and any other fees required by this submission. If the Examiner has any questions regarding this communication, or feels that an interview might facilitate prosecution of the application, he is invited to contact the undersigned at (949) 737-2900.

Respectfully submitted,
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Dated: January 21, 2004

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